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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/581,223	EHRHARDT ET AL.	
	Examiner	Art Unit	
	EILEEN B. O HARA	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *5-9,17,19 and 21-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,10-16,18 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/1/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Change of Examiner and Art Unit

1. The Examiner of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Eileen O'Hara.

Status of Claims

2. 1-35 are pending in the instant application.

Election/Restriction

3. Applicant's election with traverse of Group V in the reply filed April 24, 2009 is acknowledged. The traversal is made on the basis that because the application is a national stage filing pursuant to 35 U.S.C. § 371, unity of invention under PCT Rule 13.1 and 13.2 is the applicable standard.

Applicant writes:

"Unity of invention is fulfilled "when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical feature. The expression "special technical feature" shall mean those technical features that define a contribution which each of thc claimed inventions, considered as a whole, makes over the prior art." (PCT Rule 13.2).

The Examiner describes the technical feature linking the groups as a polypeptide having 2 methyl-6-sotanylbenzoquinone methylytransferase (activity) or a nucleic acid encoding such a polypeptide or a compound with herbicidal or growth regulatory activity that is a substrate for a 2-methyl-6-solanylbenzoquinone methyltransferase. The Examiner argues that the inventions of Group I-LX lack the same or corresponding special technical feature, because a nucleic acid allegedly 100% identical to SEQ ID NO: 3 was known, citing to Motohashi *et aL* (Genbank Accession AB054257). Applicants respectfully disagree that the instant invention does not make a contribution over the reference cited by the Examiner.

As stated in the specifieation and repeated in the claims, the general inventive concept of the present invention when considered as a whole relates to the use of 2-methyl-6-solanylbenzoquinone methyltransferase as a target for herbicides (page 1, lines 3-5). Motohashi *et al.* discloses *anArabidopsis thaliana* mRNA for APG1 and the corresponding amino acid sequence. Motohashi *et al.* does not disclose 2-methyl-6-solanylbenzoquinone methyltransferase. Motohashi *et al.* does not disclose that the APG1 mRNA encodes a polypeptide with 2-methyl-6-solanylbenzoquinon~ methyltransferase activity, nor does it disclose the use of 2-methyl-6-solanylbenzoquinone methyltransferase as a target for herbicides, Theretbre the special technical feature of the present invention makes a contribution over the reference cited by the Examiner.

Furthermore, unity of invention was found during the International stage. As shown in the International Preliminary Examination Report and International Search Report, the claims were searched and examined together. As described in MPEP § 1850 subsection t, the unity of invention standard applicable to the international stage is equally applicable during the national stage. Furthermore in MPEP § 1850 subsection II, "the decision with respect to unity of invention rests with the international Searching Authority or the International Preliminary Searching Authority," The International Searching Authority and the International Preliminary Searching Authority applying the correct standard for unity of invention under PCT Rules 13.1 and 13.2 found that unity exists.

Moreover, PCT Article 27 entitled "National Requirements," provides in part "(1) No national law shall require compliance with requirements relating to form or contents of the international application different from or additional to those which are provided for in this Treaty and the Regulations." Thus under PCT Article 27(1), the issue of lack of unity of invention should not be raised in the national phase of a PCT application when the issue was not raised during the PCT phase. Because there was no lack of unity rejection during the international phase by either the International Searching Authority or the International Preliminary Searching Authority, such a restriction is unjustified in the national phase of the present application.

Additionally, the Examiner has also required restriction between product and process claims (see Office Communication dated March 24, 2009, p. 9). However, under the applicable standard, claims directed to a product and a process of making and of using said product are an acceptable combination of categories pursuant to 37 CFR § 1.475(b)(3). Accordingly, Applicants respectfully request that the Examiner reconsider the restriction requirement for this additional reason.

Alternatively, at least Groups I-VIII (claims 1-4) and Groups XXIII-XXX (claims 10-16, 18 and 20) should be examined together. Both groupings (Groups I-VIII and Groups XXtII-XXX) relate to a method for identifying herbicides or herbicidally active substances comprising utilizing a 2-methyl-6-solanylbenzoquinone methyltransferase. Thus, Groups I-VIII and Groups XXIII-XXX are linked as to form a single general inventive concept and share the same and corresponding technical feature. Furthermore, a search of Groups I-VIII drawn to a method for identifying herbicides comprising utilizing a 2-methyl-6-solanylbenzoquinone methyltran~fersse

would be equally applicable to the claims of Groups XXII-XXX drawn to a method for identifying herbicidally active substances comprising utilizing a polypeptide with 2-methyl-6-solanylbenzoquinone methyltransferase activity. A search of claims drawn to a method for identifying herbicides comprising utilizing a 2-methyl-6-solanylbenzoquinone methyltransferase and a search of claims drawn to a method for identifying herbicidally active substances comprising utilizing a polypeptide with 2-methyl-6-solanylbenzoquinone methyltransferase activity would be commensurate in scope. Accordingly, Applicants respectfully request that the Examiner reconsider the restriction requirement and examine at least the claims of Groups I-VIII and Groups XXIII-XXX in one application.

Additionally, with the election of SEQ ID NO: 5 and its corresponding amino acid sequence SEQ ID NO: 6, all claims reciting SEQ ID NOs: 5-6 share the same feature. The same art relevant to SEQ ID NO: 5 or a nucleic acid encoding SEQ ID NO: 6 would also be relevant to products comprising SEQ ID NO: 5 or a nucleic acid encoding SEQ ID NO: 6, and to methods ofusing SEQ ID NO: 5 or a nucleic acid encoding SEQ ID NO: 6. Applicants believe that there is no undue burden on the Examiner to search all the claims which recite the elected sequences in one application, as they all relate to the same elected sequences.

Applicants' arguments are considered persuasive in part. Because the nucleic acid sequences of SEQ ID NOS: 5 and 7 are truncated versions of the nucleic acid sequence of SEQ ID NO: 3, and amino acid sequences of SEQ ID NOS: 6 and 8 are truncated versions of the full-length sequence of SEQ ID NO: 4, all of these sequences are being examined together. However, the inventions listed as Groups I-LX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features, because the claimed inventions, considered as a whole, do not make a contribution over the prior art (see rejections under 35 USC § 103).

The requirement is still deemed proper and is therefore made FINAL.

Claims 5-9, 17, 19 and 21-35 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on June 1, 2006 is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Objections

Claims 2, 3, 12 and 20 and objected to because of the following informalities: they recite non-elected inventions (SEQ ID NOS: 1 and 2). Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-4 are indefinite because Claims 1-4 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. There are no method steps present in the claims, such as: contacting either an organism or a polypeptide with a test compound and determining whether activity, growth, development, etc are reduced or affected, control steps, etc.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1) Claims 10, 11, 12, 13, 18 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying herbicidally active substances comprising bringing a polypeptide with the activity of a 2-methyl-6-solanylbenzoquinone methyltransferase into contact with test compounds or a test compound and determining whether it binds to the polypeptide or reduces or blocks the activity of the polypeptide, does not reasonably provide enablement for the same method wherein the test compound reduces or blocks ***transcription, translation or expression*** of the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A compound that would reduce or block transcription, translation or expression of a 2-methyl-6-solanylbenzoquinone methyltransferase could not be identified using the polypeptide having 2-methyl-6-solanylbenzoquinone methyltransferase activity, since the polypeptide would not be the target of the method. Such a compound would either affect transcription, such that it would be a transcription modulator, or would affect translation mechanisms, so that either a DNA translation system or a translation system would be required.

2) Claims 2, 3, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 2, 3, 11 and 12 are drawn to a method for identifying herbicides comprising using a functional equivalent of the nucleic acid of SEQ ID NO: 3 with at least 59% identity with SEQ ID NO: 4. The specification describes a polypeptide sequence consisting of SEQ ID NO: 4, which is shown to have 2-methyl-6-solanylbenzoquinone methyltransferase activity. However, the claims as written include polypeptides comprising homologues, encompass polypeptides that vary substantially in length and also in amino acid composition. The instant disclosure of a single polypeptide, that of SEQ ID NO: 4 with the instantly disclosed specific activities, does not adequately support the scope of the claimed genus, which encompasses a substantial variety of subgenera. A genus claim may be supported by a representative number of species as set forth in *Regents of the University of California v Eli Lilly & Co,* 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), which states:

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

"To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention". Lockwood v. American Airlines, Inc., 107 F.3d 1565,

1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1980) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed.") Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d 1565, 1572, 41 USPQ2d at 1966.

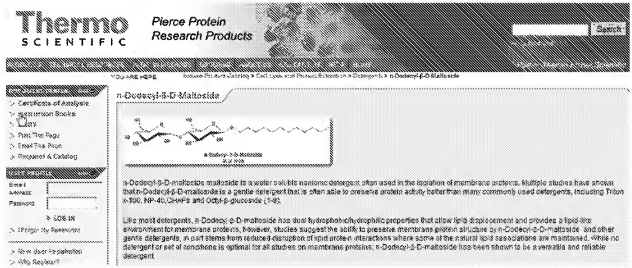
Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated nucleic acids encoding the polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 4, but not the full breadth of the claims meet the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

3) Claims 3, 4, 11, 12, 13 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying herbicidally active substances that would reduce the activity of a full-length 2-methyl-6-solanylbenzoquinone ethyltransferase of the protein of SEQ ID NO: 4 which can be encoded by the nucleic acid molecule of SEQ ID NO: 3, either using the protein of SEQ ID NO: 4 in screening assays, or by transforming plants with the nucleic acid of SEQ ID NO: 3 and screening the plants, does not reasonably provide enablement for the methods using truncated nucleic acids encoding truncated proteins, such as for example SEQ ID NOS: 5 and 7 encoding SEQ ID NOS: 6 and 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. 2-methyl-6-solanylbenzoquinone methyltransferases are membrane bound proteins found in the chroloplast inner envelope membranes. Cheng et al., The Plant Cell, 15 (October 2003), pp 2343-2356, cited as reference CF in IDS filed June 1, 2006, cloned and expressed in E. coli the full-length vte3 protein-coding region from Arabidopsis (which is identical to the protein of SEQ ID NO: 4 of the instant application), and assayed the protein for in vitro activity to determine substrate specificity (pages 2349-2350, Fig. 5). The protein was solubilized and assayed in Tween 20, β-D-dodecyl-maltoside, 3-[(3-Cholamidopropyl)-dimethylammonio}-1-

propanesulfonic acid and Triton X-100, all of which are detergents used to solubilize and maintain activity of membrane bound proteins. For example, see the Web page for Thermo Scientific for β-D-dodecyl-maltoside, in which studies have shown that the ability to preserve membrane protein structure by n-Dodecyl-b-D-maltoside, and other gentle detergents, in part stems from reduced disruption of lipid:protein interactions where some of the natural lipid associations are maintained.



The transmembrane domain for the protein of SEQ ID O: 4 is located at the C terminus, and therefore deleting the C terminus would remove the transmembrane domain. Since the transmembrane domain is often necessary for activity of a membrane bound protein involved in the synthesis of lipid soluble compounds (tocopherols, collectively termed vitamine E), 2-methyl-6-solanylbenzoquinone methyltransferases would not be expected to be active without their transmembrane domain, as evidenced by Cheng et al. Therefore, a truncated protein of SEQ ID NO: 4, such as SEQ ID NO: 6 or 8, would not likely to function in either an in vitro

assay, or in an in vivo assay using a plant expressing a truncated protein. In addition, the claims also require truncation of the N-terminus, which alone or in conjunction with a truncation of the C terminus, render the protein inactive.

The instant specification does not identify those regions of the amino acid sequence of SEQ ID NO:4 which are essential for its biological activity and structural integrity and those regions which are either expendable or substitutable. While it is known that truncations at the N and/or C terminus of a protein may be made while retaining the activity of a protein, ertain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Proteins lacking these regions may have no or reduced activity. However, Applicant has provided little or no guidance beyond disclosing that N and C-terminal truncated proteins of SEQ ID NO: 4 may be expressed and isolated from E. coli, however, there is no data that these truncated proteins retain activity. Experiments in the specification were performed with the nuclei acids encoding the full-length protein.

There are many factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue. These factors include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of

experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (FED. Cir. 1988).

It is acknowledged that the level of skill in the art is high. However, due to the lack of lack of direction/guidance in the specification as to how many or if any amino acids could be deleted from the C and/or N terminus and still have a protein retaining activity and absence of examples, the art which teaches assaying the full-length protein in detergents which maintain a lipid environment, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-4 and 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motohashi et al, Database EMBL, Accession No. Q94IE2, 12/01/2001, cited as reference CC in IDS filed June 1, 2006, in view of Cheng et al., The Plant Cell, 15 (October 2003), pp 2343-2356, cited as reference CF in IDS filed June 1, 2006, and further in view of Coughlan, U.S. Patent No. 7,071,381, priority date 6/4/2001, and evidenced by the ABRC website, papers 1, 2 and 3, and further in view of Zander et al, U.S. Patent No. 6,261,803 and Sharma et al, U.S. Patent No. 5,728,804.

Claims 1-4 and 10-16 are drawn to methods of identifying herbicidally active substances that would reduce the activity of a 2-methyl-6-solanylbenzoquinone methyltransferase which can be encoded by the nucleic acid molecule of SEQ ID NO: 3, 5 or 7 or which encodes the polypeptide of SEQ ID NO: 4, 6 or 8 or truncated versions thereof wherein the truncated polypeptides are truncated by at least 20 amino acids at both the C terminus, comprising administering a test compound or compounds to a transgenic or non-transgenic organism comprising the 2-methyl-6-solanylbenzoquinone methyltransferase, or cell digests thereof comprising the 2-methyl-6-solanylbenzoquinone methyltransferase, and determining whether the

2-methyl-6-solanylbenzoquinone methyltransferase is reduced or blocked or whether transgenic organism over-expressing 2-methyl-6-solanylbenzoquinone methyltransferase has a reduced growth rate or a reduced viability in comparison with the non-transgenic organism of the same type, or by contacting a 2-methyl-6-solanylbenzoquinone methyltransferase polypeptide with a test compound or compounds, and determining whether it binds to the polypeptide or reduces or blocks the activity of the polypeptide.

Motohashi et al discloses the protein apg1, which is 100% identical to the full-length protein of SEQ ID NO: 3 of the instant invention, and that it is a membrane protein. Motohashi et al does not disclose the activity of the protein.

Cheng et al discloses that the vte3 gene encodes a 2-methyl-6-solanylbenzoquinone methyltransferase, which is identical to the protein of Motohashi et al, and that the protein can be screened for activity in vitro (see abstract, pages 2349-2350). See also ABRC website, papers 1, 2 and 3, which show that apg1 and vte3 are the same proteins.

Coughlan teaches that enzymes involved in vitamin E, such as methyltransferases, may be used to discover new herbicides, since those enzymes are not found in mammals.

At paragraph 37 Coughlan writes:

> "The nucleic acid fragments of the instant invention may be used to create transgenic plants in which the disclosed polypeptides are present at higher or lower levels than normal or in cell types or developmental stages in which they are not normally found. This would have the effect of altering the level of homogenistate in those cells. Overexpression of 4-hydroxyphenylpyruvate dioxygenase should result in a larger accumulation of homogenistate which may be used by gamma tocopherol methyltransferase to produce vitamin E. Since mammals can not synthesize tocopherols, the enzymes described herein may be used for the discovery of new herbicides."

Sharma et al teaches the problems associated with producing eukaryotic proteins in bacteria, in which the eukaryotic proteins can aggregate due to hydrophobic residues.

At paragraph 4 Sharma et al. writes:

(4) The cellular environment of a human cell however, is very different from that of a bacterium, and the production of human protein pharmaceuticals in bacteria by genetic engineering often results in the accumulation of improperly folded proteins (called inclusion bodies) which have little or no biological activity. See, for example, J. L. Cleland, ed., Protein Folding, In Vivo and In Vitro, ACS Syrup. Series, 526 (1993). The current hypothesis of protein folding involves the formation of one or more intermediates from the unfolded protein. These intermediates seem to possess some secondary structure and often associate to form soluble aggregates. The soluble protein aggregates can agglomerate to form large irreversible precipitates which appear as " inclusion bodies" in bacterial cells. All intermediates as well as the unfolded protein can form misfolded intermediates that can reduce the yield of the native protein by becoming a kinetic trap for the preceding species. There is considerable evidence that the intermediates have many hydrophobic amino acid residues exposed to the surface which causes their aggregation. These proteins, after isolation and purification from the host cells, have to be completely unfolded, or denatured, and subsequently refolded or renatured so that the proteins regain their bioactivity. However, since every protein has a different three dimensional structure, the folding of a protein from a completely unfolded state to the native conformation it requires to be functional, remains a complex problem.

Zander et al. teaches that expression of human membrane proteins is lower than expression of soluble proteins, and suggests that deleting the nucleic acids encoding the transmembrane domain would be one solution for this problem (see paragraphs 5-7).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use the apg1 protein of Motohashi et al, or a transgenic organism expressing the apg1 protein, as targets for testing compounds for potential herbicides. Cheng et al. teaches that the apg1 (vte3) protein is a 2-methyl-6-solanylbenzoquinone methyltransferase (MSBQ MT), and also teaches in vitro assays that can be used to discover potential substrates, and Coughlan teaches that methyltransferases used to produce vitamin E could be used to discover new

herbicides in transgenic plants, since these enzymes are not present in mammals and therefore would not be toxic to humans. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to arrive at the instant invention by the combination of these references. It would also have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a protein having a truncation at the C terminus, since this is where the transmembrane domain is located, and Sharma et al and Zander et al teach that hydrophobic residues of eukaryotic proteins can cause protein aggregation if produced in bacteria, and that one solution would be to remove the transmembrane region. There would have been a reasonable expectation of success, since making recombinant proteins and transgenic plants were common and well known in the art, as were screening methods.

Further, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007), that "a person of ordinary skill attempting to solve a problem will" not " be led only to those elements of prior art designed to solve the same problem……" (KSR, 550 U.S. at_, 82 USPQ2d at 1397). In addition, the court found that "When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary skill can implement a predictable variant, 35 USC 103 likely bars its patentability" (KSR, 550 U.S. at_, 82 USPQ2d at 1396). Further the court found that the Federal Circuit has erred in applying the teaching-suggestion-motivation test in an overly rigid and formalistic way, in particular by concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try'" (KSR, 550 U.S. at_, 82 USPQ2d at 1397) and has further determined that "…….[t]he combination of familiar elements according to known

methods is likely to be obvious when it does no more than yield predictable results" (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that "…… the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious" (KSR, 550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions" ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to screen for herbicides using the 2-methyl-6-solanylbenzoquinone methyltransferase protein or organisms comprising the protein, since this would be a desirable target because a compound specifically targeting this protein would not affect mammals. Coughlan Albanell specifically recognized the problem or need in the art to solve the problem of finding new herbicides that would not be toxic to mammals. Further, given the known problem to be solved, given the known conventional and successful techniques for solving the problem, given that Coughlan provides a specific identified, predictable, potential solution to the recognized problem, the variation of the technique of Coughlan to specifically use 2-methyl-6-solanylbenzoquinone methyltransferase protein is obvious.

Finally, given the above, the claimed invention is obvious over the prior art because it would have been obvious to screen for herbicides using 2-methyl-6-solanylbenzoquinone methyltransferase protein by known methods and suggested by Coughlan with a reasonable

expectation of success, wherein the success of the solution would be a product of ordinary skill and common sense but not the product of innovation.

Claims 18 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Motohashi et al, Database EMBL, Accession No. Q94IE2, 12/01/2001, cited as reference CC in IDS filed June 1, 2006, in view of Cheng et al., The Plant Cell, 15 (October 2003), pp2343-2356, cited as reference CF in IDS filed June 1, 2006, in view of Coughlan, U.S. Patent No. 7,071,381, priority date 6/4/2001, Zander et al, U.S. Patent No. 6,261,803 and Sharma et al, U.S. Patent No. 5,728,804, and further in view of Parce et al, U.S. Patent No. 7,037416.

Claims 18 and 20 are drawn to methods of identifying herbicidally active substances that would reduce the activity of a 2-methyl-6-solanylbenzoquinone methyltransferase which can be encoded by the nucleic acid molecule of SEQ ID NO: 5 or 7 or which encodes the polypeptide of SEQ ID NO: 6 or 8 or truncated versions thereof wherein the truncated polypeptides are truncated by at least 20 amino acids at both the C terminus, comprising contacting a 2-methyl-6-solanylbenzoquinone methyltransferase polypeptide with a test compound or compounds, and determining whether it binds to the polypeptide or reduces or blocks the activity of the polypeptide, wherein the test compound is identified by high-throughput screening.

The teachings of Motohashi et al, Cheng et al, Coughlan, Zander and Sharm are described above. These references do not teach a method of high-throughput screening for test compounds.

Parce teaches methods a high-throughput methods of screening, for example for inhibitors of a enzyme. At paragraph 2 Parce et al. states:

"(2) Biological assays are often performed in high-throughput systems to screen a large number of different compounds for their effect on a biological system, e.g., to screen a plurality of potential enzyme inhibitors. Many of these assays, e.g., enzyme assays, are performed in microfluidic devices as described, e.g., in a number of issued patents and published PCT applications. For example, microfluidic methods of performing biological assays in microfluidic systems have been developed, such as those described by the pioneering applications of Parce et al., "High Throughput Screening Assay Systems in Microscale Fluidic Devices" WO 98/00231 and in Knapp et al., "Closed Loop Biochemical Analyzers" (WO 98/45481)."

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to use a high-throughput screen for herbicidally active compounds against methyltransferases that are involved with production of vitamin E, as taught by Coughlan, using the apg1 protein of Motohashi et al., since Cheng et al. teaches that the apg1 protein is a 2-methyl-6-solanylbenzoquinone methyltransferase. Parce et al. teaches that biological assays are often performed in high-throughput systems in order to screen large numbers of different compounds, making the screening time and cost efficient. There would be reasonable expectation of success, since Parce et al. teaches that there is extensive literature on how to do high-throughput assays, and they have been extensively and successfully used in the biological sciences.

Further, the Supreme Court has determined, in *KSR International Co. v. Teleflex, Inc.*, 550 U.S._, 82, USPQ2d 1385 (2007), that "a person of ordinary skill attempting to solve a problem will" not " be led only to those elements of prior art designed to solve the same problem....." (KSR, 550 U.S. at_, 82 USPQ2d at 1397). In addition, the court found that "When a work is available in one field of endeavor, design incentives and other market forces can prompt variations of it, either in the same field or a different one. If a person of ordinary

skill can implement a predictable variant, 35 USC 103 likely bars its patentability" (KSR, 550 U.S. at_, 82 USPQ2d at 1396). Further the court found that the Federal Circuit has erred in applying the teaching-suggestion-motivation test in an overly rigid and formalistic way, in particular by concluding "that a patent claim cannot be proved obvious merely by showing that the combination of elements was 'obvious to try'" (KSR, 550 U.S. at_, 82 USPQ2d at 1397) and has further determined that ".....[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results" (KSR, 550 U.S. at_, 82 USPQ2d at 1395). The court further found that "..... the conclusion that when a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious" (KSR, 550 U.S. at_, 82 USPQ2d at 1395-1396). Thus, when considering obviousness of a combination of known elements, the operative question is "whether the improvement is more than the predictable use of prior art elements according to their established functions" ((KSR, 550 U.S. at_, 82 USPQ2d at 1396).

Given the above, applying the same logic to the instant process claims, it would have been *prima facie* obvious to screen for herbicides using a high-throughput system, since this is a standard system used in biological research. Further, given the known problem to be solved, given the known conventional and successful techniques for solving the problem, given that Parce et al. provides a specific identified, predictable, potential solution to the recognized problem, the variation of the technique of Coughlan to use a high-throughput system is obvious.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara whose telephone number is (571) 272-0878. The examiner can normally be reached on 9:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Eileen B. O'Hara/
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Art Unit 1638